SPIRODICLOFEN (237)

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EXPLANATION

Spirodiclofen, a ketoenol (tetronic acid) insecticide was evaluated for the first time by the 2009 JMPR, where an ADI of 0–0.01 mg/kg bw was established and it was agreed that an ARfD was not necessary, residue definitions were proposed and maximum residue levels were recommended for a number of uses where GAP and supporting information were available.

The 2009 JMPR established residue definitions for spirodiclofen:

- For plant products (compliance with MRLs and dietary intake estimation): *spirodiclofen*

- For animal products (compliance with MRLs): *spirodiclofen (fat soluble)*

- For animal products (dietary intake assessment): *sum of spirodiclofen and spirodiclofen-enol, expressed as spirodiclofen.*

Spirodiclofen was listed by the Forty-fifth Session of the CCPR (2013) for the review of additional maximum residue levels for blueberries and avocados and the 2014 JMPR received GAP and residue information for these crops.

METHODS OF RESIDUE ANALYSIS

Analytical methods

The 2009 JMPR reviewed and summarised analytical method descriptions and validation data for spirodiclofen and some of its metabolites in crop, processed commodities and animal commodities, including the HPLC/MS-MS multi-residue method 109351 (validated for the determination of parent spirodiclofen in plant commodities with high acid content, high water content and high fat content) and the HPLC/MS-MS method BA-001-P06-01 (validated for the determination of parent spirodiclofen and metabolites (3) in apples, grapes and their processed fractions).

The analytical method used in the supervised residue trials on blueberry was a modification of Method 109351 (i.e., without the ENVI-Carb or amino-cartridge clean-up steps) and involved extraction with acetonitrile/water/20% cysteine hydrochloride (200:100:1), filtration with Celite, acidification with HCl, partitioning into dichloromethane, evaporation and re-suspension acetonitrile/formic acid prior to analysis by HPLC/MS-MS (triple-quad, positive MRM mode). The reported LOQ of this method was 0.01 mg/kg. [Ref: 109351-1]

Table 1 Recoveries of spirodiclofen with HPLC/MS-MS method 109351

Commodity	LOQ (mg/kg)	Recovery type	spike level (mg/kg)	recoveries % range (mean)	SD (n)	Reference
blueberry	0.01	validation	0.01 0.2 5.11	88-120 (103) 93-100 (97) 93-103 (97)	16 (3) 4 (3) 5 (3)	IR4 PR-09679
		procedural	0.01 5.11	81-109 (93) 85-98 (92)	9 (14) 4 (14)	

Samples from the supervised trials on avocados were analysed using a modification of the HPLC/MS-MS Method BA-001-P06-01 (i.e., with the addition of cysteine hydrochloride to the acetonitrile/water extraction solvent) and involved acetonitrile/water extraction, the addition of isotopic internal standards and filtration prior to analysis for parent spirodiclofen by HPLC/MS-MS (positive MRM mode). The reported LOQ of this method was 0.01 mg/kg. [Ref: BA-001-P06-01

Table 2 Recoveries of spirodiclofen with HPLC/MS-MS method BA-001-P06-01

Commodity	Reported LOQ (mg/kg)	Recovery type	spike level (mg/kg)	recoveries % range (mean)	SD (n)	Reference
avocado	0.01	validation	0.01	100-116 (109)	5 (7)	RABAP001
		procedural	0.01 0.5 1.0	93-109 (101) 95-101 (98) 98-105 (101)	6 (2) 3 (3) 4 (3)	

Stability of residues in stored analytical samples

The 2009 JMPR reviewed freezer storage stability studies on a range of representative substrates and concluded that spirodiclofen was stable when stored frozen for at least 13 months in crops with high water content (peach), at least 24 months in crops with high acid content (citrus, grapes), 16 months in crops with oil content (almond nutmeat, dry hop cones), at least 8 months in fruit juice (apple juice, grape juice), and at least 10 months in dried fruit (dried apples, raisins, dried plums).

The Meeting received additional spirodiclofen storage stability studies on blueberry [Ref: IR4 PR-09679] where untreated samples from the field trials were fortified with 0.2 mg/kg spirodiclofen and stored for 47–51 weeks at or below -12 °C.

Samples were taken for extraction and analysis after 47–51 weeks, with the stored control samples being freshly fortified and analysed concurrently to determine the procedural recovery efficiency. Analysis was by LC-MS/MS (Method 109351, with procedural recovery rates of 78–101% in samples fortified at 0.01 mg/kg to 5.1 mg/kg). After 47–51 weeks storage, measured residues of spirodiclofen in stored samples were 85% of the spiked level.

Table 3 Stability of residues in plant matrices fortified with spirodiclofen and stored at ≤ -4 °C

Commodity	Fortification (mg/kg)	Storage interval (weeks)	Spirodiclofen residues (mg/kg)	% Remaining	Procedural recovery (%)
blueberry	0.2	47	0.18, 0.18, 0.17	85	82% at 0.01 mg/kg) 81% (at 0.2 mg/kg) 87% at 5.1 mg/kg)

USE PATTERNS

Information on GAP in USA was provided to the Meeting for foliar applications to blueberries and avocados and these are summarised in Table 4.

Table 4 Registered uses of spirodiclofen (240 g ai/litre SC formulation)

Crop	Country	Application				Max/season		PHI (days)	Remarks:
		method	kg ai/ha	kg ai/hL	water L/ha	no	kg ai/ha		
Bush berries (004B)									
Blueberries	Canada	spray	0.31		100-1000	1	0.31	7	
Assorted tropical and sub-tropical fruits – inedible peel-large (006B)									
Avocado [a]	USA	spray	0.31-0.35		468	1	0.35	2	

[a] GAP is for Avocados and also Black sapote, Canistel, Mamey sapote, Mango, Papaya, Sapodilla, Star apple.

RESIDUES RESULTING FROM SUPERVISED TRIALS

The Meeting received new information on supervised field trials involving foliar applications of spirodiclofen to the following crops.

Crop group	Code	Crop	Source	Table
Bush berries	004B	Blueberries	USA, Canada	Table 5
Assorted tropical and sub-tropical fruits – inedible peel (large)	006B	Avocado	USA	Table 6

The supervised trials were well documented with laboratory and field reports. Laboratory reports included method validation including procedural recoveries with spiking at residue levels similar to those occurring in samples from the supervised trials. Dates of analyses or duration of residue sample storage were also provided. Although trials included control plots, no control data are recorded in the tables unless residues in control samples exceeded the LOQ. Residue data are recorded unadjusted for recovery.

Intervals of freezer storage between sampling and analysis were recorded for all trials and were covered by the conditions of the freezer storage stability studies.

Results from replicated field plots are presented as individual values. When residues were not detected they are shown as below the LOQ (e.g., < 0.01 mg/kg). Residues and application rates have been rounded to two significant digits (or if close to the LOQ, rounded to one significant digit). Average values and proportionally adjusted residues have been calculated from the residue results prior to rounding and the results from trials used for the estimation of maximum residue levels have been (underlined).

Bush berries

Blueberries

Results from supervised trials from USA and Canada on highbush and lowbush blueberries were provided to the Meeting. In these trials, one foliar application of spirodiclofen (SC 240 formulation) was applied without spray adjuvant to mature bushes using backpack 1–6 nozzle boom sprayers or tractor-mounted airblast sprayer. Plot sizes in these trials ranged from 33–167 square metres.

Duplicate samples of at least 0.9 kg fruit were taken from at least 12 bushes/plot at maturity or when 70–80% of fruit were ripe, frozen within 24 hours of sampling and stored at -12 °C for up to 327 days before berries were extracted and analysed for spirodiclofen using LC/MS/MS Method 109351 within 1 day of extraction. The reported LOQ was 0.01 mg/kg and the mean recovery rates in samples spiked with 0.01–0.5 mg/kg spirodiclofen ranged from 81–109%.

Table 5 Residues on blueberries (highbush and lowbush) from trials in Canada and USA involving one foliar application of spirodiclofen (240 SC formulation)

BLUEBERRIES Country, year Location (variety)	Application			Matrix	DAT	Residues (mg/kg)		Reference & Comments
	kg ai/ha	water (L/ha)	kg ai/hL			Spirodiclofen	mean	
GAP: Canada	1 ×0.31	100-1000			7			max 0.31 kg ai/ha/season
Canada, 2006 Agassiz, BC (Bluecrop)	0.32	178	0.18	berries	6	1.1, 1.0	1.1	IR4 PR-09679 Trial 06-BC08
USA, 2006 Fennville, MI (Rubel)	0.31	617	0.051	berries	8	0.4, 0.36	0.38	IR4 PR-09679 Trial 06-M131 [airblast]
USA, 2006 Jonesboro, ME (Lowbush-wild)	0.32	374	0.084	berries	7	0.67, 1.0	0.84	IR4 PR-09679 Trial 06-ME03

BLUEBERRIES Country, year Location (variety)	Application			Matrix	DAT	Residues (mg/kg)		Reference & Comments
	kg ai/ha	water (L/ha)	kg ai/hL			Spirodiclofen	mean	
USA, 2006 Castle Hayne, NC (Croatan)	0.31	384	0.081	berries	1 3 7 10 14	0.87, 0.76 0.79, 0.61 0.45, 0.55 0.39, 0.46 0.34, 0.27	0.81 0.7 0.5 0.43 0.31	IR4 PR-09679 Trial 06-NC22
USA, 2006 Castle Hayne, NC (Summit)	0.32	402	0.078	berries	6	0.61, 0.55	0.58	IR4 PR-09679 Trial 06-NC23
USA, 2006 Chatsworth, NJ (Bluecrop)	0.32	421	0.076	berries	6	0.85, 0.55	0.7	IR4 PR-09679 Trial 06-NJ28
Canada, 2006 Kentville, NS (Lowbush-wild)	0.34	440	0.078	berries	1 3 6 9 14	3.1, 2.9 3.3, 3.2 2.3, 2.3 2.1, 2.1 1.4, 1.8	3.0 3.3 2.3 2.1 1.6	IR4 PR-09679 Trial 06-NS06
Canada, 2006 Kentville, NS (Lowbush-wild)	0.34	430	0.078	berries	7	1.5, 1.5	1.5	IR4 PR-09679 Trial 06-NS07
Canada, 2006 Kentville, NS (Lowbush-wild)	0.34	440	0.078	berries	6	1.4, 1.6	1.5	IR4 PR-09679 Trial 06-NS08
USA, 2006 Aurora, OR (Bluecrop)	0.32	290	0.11	berries	6	0.56, 0.46	0.51	IR4 PR-09679 Trial 06-OR24 [Mostly green berries]
Canada, 2006 St-David-de-Falardeau , QC (Lowbush-wild)	0.3	290	0.1	berries	7	1.0, 0.97	0.99	IR4 PR-09679 Trial 06-QC07
Canada, 2006 Labreque, QC (Lowbush-wild)	0.32	299	0.11	berries	7	1.1, 1.2	1.1	IR4 PR-09679 Trial 06-QC08

Assorted tropical and sub-tropical fruits – inedible peel- large (006B)

Avocado

Results from supervised trials from USA on avocado were provided to the Meeting. In these trials, one foliar application of spirodiclofen (SC 240 formulation) was applied without spray adjuvant, as either a dilute spray (1800–3700 litres/ha) or a concentrate spray (330–650 litres/ha) to mature trees using airblast sprayers. Plot sizes in these trials ranged from 125–372 square metres with a minimum of 4 trees.

Duplicate samples of at least 2 kg mature fruit were frozen within 9 hours of sampling and stored at -15 °C for up to 10 months before whole fruit were extracted and analysed for spirodiclofen using LC/MS/MS Method BA-001-P06-01 within 4 days of extraction. The reported LOQ was 0.01 mg/kg and the mean recovery rates in samples spiked with 0.01–1.0 mg/kg spirodiclofen ranged from 98–101%.

Table 6 Residues on avocado from trials in USA involving one foliar application of spirodiclofen (240 SC formulation)

AVOCADO Country, year Location (variety)	Application			Matrix	DAT	Residues (mg/kg)		Reference & Comments
	kg ai/ha	water (L/ha)	kg ai/hL			Spirodiclofen	mean	
GAP: USA	1×0.35				2			max 0.35 kg ai/ha/season
USA, 2007 Canal Point, FL (Tonnage)	0.35	2241	0.016	fruit	2	0.18, 0.2	0.19	RABAP001 BA001-07-HA-A
	0.35	511	0.068	fruit	2	0.33, 0.61	<u>0.47</u>	RABAP001 BA001-07-HA-B
USA, 2007 Carpenteria, CA (Haas)	0.35	2338	0.015	fruit	2	0.02, 0.12	<u>0.07</u>	RABAP001 BA004-07-HA-A 12 yr trees 26 Jul application BBCH 85
	0.35	468	0.075	fruit	2	< 0.01, < 0.01	< 0.01	RABAP001 BA004-07-HA-B
USA, 2007 Carpenteria, CA (Haas)	0.35	2125	0.016	fruit	2	0.03, 0.05	<u>0.04</u>	RABAP001 BA005-07-HA-A 27 yr trees 17 Aug application BBCH 89
	0.35	427	0.082	fruit	2	0.02, 0.01	0.015	RABAP001 BA005-07-HA-B
USA, 2008 San Luis Obispo, CA (Haas)	0.37	3390	0.011	fruit	2	0.11, 0.12	0.12	RABAP001 BA002-07-DA-A
	0.35	652	0.054	fruit	0 2 5 7 10	0.25, 0.16 0.13, 0.08 0.15, 0.15 0.15, 0.14 0.11, 0.07	0.21 0.11 <u>0.15</u> 0.15 0.09	RABAP001 BA002-07-DA-B
USA, 2007 Arroyo Grande, CA (Tonnage)	0.36	2041	0.017	fruit	2	0.06, 0.06	0.06	RABAP001 BA003-07-DA-A
	0.36	460	0.077	fruit	0 2 5 7 10	0.12, 0.11 0.08, 0.05 0.02, 0.03 0.03, 0.03 0.03, 0.01	0.12 <u>0.07</u> 0.03 0.03 0.02	RABAP001 BA003-07-DA-B

APPRAISAL

Spirodiclofen, a ketoenol (tetronic acid) insecticide was evaluated for the first time by the 2009 JMPR, where an ADI of 0–0.01 mg/kg bw was established and it was agreed that an ARfD was not necessary. Residue definitions were proposed and maximum residue levels were recommended for a number of uses where GAP and supporting information were available.

Residue definitions established by the 2009 JMPR are:

- For plant products (compliance with MRLs and dietary intake estimation): *spirodiclofen*
- For animal products (compliance with MRLs): *spirodiclofen (fat soluble)*
- For animal products (dietary intake assessment): *sum of spirodiclofen and spirodiclofen-enol, expressed as spirodiclofen.*

Spirodiclofen was listed by the Forty-fifth Session of the CCPR (2013) for the review of additional MRLs for blueberries and avocados and the 2014 JMPR received GAP and residue information for these crops.

Methods of analysis

The 2009 JMPR reviewed and summarised analytical method descriptions and validation data for spirodiclofen and some of its metabolites in crop, processed commodities and animal commodities, including the HPLC-MS-MS multi-residue method 109351 (validated for the determination of parent spirodiclofen in plant commodities with high acid content, high water content and high fat content) and the HPLC/MS-MS method BA-001-P06-01 (validated for the determination of parent spirodiclofen and metabolites (3) in apples, grapes and their processed fractions).

These methods, with minor modifications were validated and used in the supervised residue trials on blueberry (Method 109351) and avocado (Method BA-001-P06-01) with an LOQ of 0.01 mg/kg.

Stability of residues in stored analytical samples

The 2009 JMPR reviewed freezer storage stability studies on a range of representative substrates and concluded that in stored frozen analytical samples, spirodiclofen was stable for at least 13 months in crops with high water content (peach), 24 months in crops with high acid content (citrus, grapes), 16 months in crops with oil content (almond nutmeat, dry hop cones), 8 months in fruit juice (apple juice, grape juice) and 10 months in dried fruit (dried apples, raisins, dried plums).

The Meeting received additional spirodiclofen storage stability studies on blueberry, showing that residues were stable in blueberry analytical samples stored frozen for at least 12 months.

Results of supervised residue trials on crops

The Meeting received new information on supervised field trials involving foliar applications of spirodiclofen to blueberries and avocados.

Blueberries

Results from supervised trials from USA and Canada on highbush and lowbush blueberries were provided to the Meeting.

The critical GAP for blueberries is in Canada, one application of 0.31 kg ai/ha with a PHI of 7 days. In trials from North America matching this GAP, spirodiclofen residues were: 0.38, 0.5, 0.51, 0.58, 0.7, 0.84, 0.99, 1.1, 1.1, 1.5, 1.5 and 2.3 mg/kg (n=12).

The Meeting estimated a maximum residue level of 4 mg/kg and an STMR of 0.92 mg/kg for spirodiclofen on blueberries.

Avocado

Results from supervised trials from USA on avocado were provided to the Meeting.

The critical GAP for avocados is in USA, one application of up to 0.35 kg ai/ha with a PHI of 2 days. In trials from USA matching this GAP, spirodiclofen residues were: 0.04, 0.07, 0.07, 0.15 and 0.47 mg/kg.

The Meeting estimated a maximum residue level of 0.9 mg/kg and an STMR of 0.07 mg/kg for spirodiclofen on avocado.

Farm animal dietary burden

As neither of these commodities are livestock feed items, the Meeting agreed that the 2009 JMPR conclusions and maximum residue level recommendations for livestock commodities did not need to be reviewed.

RECOMMENDATIONS

On the basis of the data from supervised trials the Meeting concluded that the residue levels listed below are suitable for establishing maximum residue limits and for IEDI assessment.

Definition of the residue for compliance with the MRL and for the estimation of dietary intake for plant commodities: *spirodiclofen*

Definition of the residue for compliance with the MRL for animal commodities: *spirodiclofen*

Definition of the residue for the estimation of dietary intake for animal commodities: *sum of spirodiclofen and spirodiclofen-enol, expressed as spirodiclofen.*

The residue is fat soluble

	Commodity	MRL (mg/kg)		STMR
CCN	Name	New	Prev	
FB 0020	Blueberry	4.0		0.92
FI 0326	Avocado	0.9		0.07

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDI) for spirodiclofen was calculated from recommendations for STMRs for raw commodities in combination with consumption data for corresponding food commodities. The results are shown in Annex 3 to the 2014 Report.

The International Estimated Daily Intakes (IEDI) of in the 17 GEMS/Food cluster diets, based on the estimated STMRs were in the range 1–8% of the maximum ADI of 0.01 mg/kg bw. The Meeting concluded that the long-term intake of residues of spirodiclofen from uses considered by the Meeting is unlikely to present a public health concern.

Short-term intake

No ARfD was considered necessary. The Meeting concluded that the short-term intake of residues of spirodiclofen from uses considered by the Meeting is unlikely to present a public health concern.

REFERENCES

Reference	Author(s)	Year	Title
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109351-1	Gould, T.J	2009	An analytical method for the determination of BAJ 2740 residue in various plant matrices by LC-MS/MS. Bayer Corporation, Stilwell, KS, USA. Bayer CropScience, Report No. 109351-1, Amended: 2009-01-12. Unpublished.
BA-001-P06-01	Netzband, D.; Yin, J.	2006	Analytical method for the determination of residues of spirodiclofen and its metabolites BAJ2510, 3-OH-enol spirodiclofen and 4-OH-enol spirodiclofen in apple and grape matrices using LC/MS/MS. Bayer CropScience LP, Stilwell, KS, USA. Bayer CropScience, Report No. BA-001-P06-01. Unpublished.
IR4 PR-09679	Dorschner, K. W.	2009	Spirodiclofen: Magnitude of the residue on blueberry. IR-4 Project HQ, Rutgers, The State University of New Jersey, Princeton, NJ, USA. Report No. IR-4 PR No. 09679, includes Trials: 06-BC08, 06-ME03, 06-MI31,06-NC22, 06-NC23, 06-NJ28, 06-NS06, 06-NS07, 06-NS08, 06-OR24, 06-QC07 and 06-QC08. Unpublished.

Reference	Author(s)	Year	Title
RABAP001	Dacus, S. C.; Hoag, R. E.	2008	Spirodiclofen - Magnitude of the residue in/on avocado. Bayer CropScience LP, Stilwell, KS, USA. Bayer CropScience, Report No.: RABAP001, includes Trial Nos: BA001-07HA-A, BA001-07HA-B, BA002-07DA-A, BA002-07DA-B, BA003-07DA-A, BA003-07DA-B, BA004-07DA-A, BA004-07DA-B, BA005-07DA-A and BA005-07DA-B, Unpublished